REMARKS

I. Claim Rejections - 35 USC § 112

The Office has maintained the rejection of claim 5 under 35 USC § 112, second paragraph, because the phrase "active truncated derivatives thereof" is unclear.

Applicant respectfully traverses this rejection. "Active truncated derivatives" is a well-known phrase referring to functional fragments of compounds. The phrase is widely used in journal publications and patents. See, for example, the claims of U.S. Patent Nos. 6,326,387, 6,284,778, 6,172,086, 6,124,328, 5,935,954, 5,888,815, 5,840,736, 5,811,434 and 5,780,484. In allowing the claims of these patents, the Office recognized that the phrase is definite within the meaning of 35 USC § 112, second paragraph.

II. Claim Rejections - 35 USC § 102

The Office has maintained the 35 USC § 102(a) rejection of claim 1 as being anticipated by Maloney et al. (*J. Med. Chem.*, July 15, 1999, Volume 42, pages 2504-2526), and the 35 USC § 102(b) rejections of claims 1 and 3-5 as being anticipated by Imbach et al. (CA 60:2923b), Wakabayashi et al. (JP 52-83686), GB 1,503,244, Liao et al. (CA 102:6312), Jamieson et al. (U.S. Patent No. 4,230,709), WO 96/06846 and López-Rodríguez (*J. Med. Chem.*, May 23, 1997, Volume 40, pages 1648-1656).

The foregoing amendments obviate the rejections over Moloney et al., Imbach et al., Wakabayashi et al., GB 1,503,244, Liao et al. and Jamieson et al.

Applicant respectfully traverses the rejection over WO 96/06846 and López-Rodríguez (*J. Med. Chem.*, May 23, 1997, Volume 40, pages 1648-1656). Both WO

96/06846 and López-Rodríguez disclose compounds containing a piperazine ring. By contrast, the instantly claimed compounds lack a piperazine ring at position R. "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). Since neither WO 96/06846 nor López-Rodríguez teaches compounds having a moiety other than piperazine at position R, the references do not anticipate claim 1.

III. Claim Rejections - 35 USC § 103(a)

The Office has maintained the 35 USC § 103(a) rejection of claims 1-5 as being obvious over Wakabayashi et al. (JP 52083686), GB 1,503,244, Jamieson et al. (U.S. Patent No. 4,230,709) and WO 96/06846.

Applicant respectfully traverses this rejection on the basis that the Office has failed to establish a *prima facie* case of obviousness.

The cited references fail to disclose the asserted utilities of the claimed compounds. The asserted utilities of the claimed compounds include stimulation of neuronal regeneration and outgrowth. See, for example, the specification at page 17, lines 11-13, and claim 6 in the application as originally filed. By contrast, Wakabayashi et al. and GB 1,503,244 disclose compounds having herbicidal and fungicidal activity; Jamieson et al. disclose compounds for treating asthma; and WO 96/06846 discloses compounds for treating anxiety and depression. Thus, none of the cited references teaches or suggests the neuroregenerative properties of the claimed compounds.

The premise underlying the obviousness rejection derives from an expectation that structurally similar compounds will have similar properties. Controlling authority holds that such expectation may not arise where the prior art fails to disclose the utility asserted for the claimed compounds. *In re Lalu*, 747 F.2d 703, 707, 223 U.S.P.Q. 1257, 1260 (Fed. Cir. 1984)(in finding no motivation to modify a reaction intermediate to obtain a structurally similar corrosion inhibiting compound, the court framed the obviousness analysis as requiring an inquiry into whether the prior art "would suggest the expected properties of the claimed compounds" or whether the prior art discloses any utility of its compounds that "would support an expectation that the claimed compounds would have similar properties"); *In re May*, 574 F.2d 1082, 197 U.S.P.Q. 601 (C.C.P.A. 1978)(the inventors' discovery of a property not disclosed by the prior art for structurally similar compounds undermined the expectation).

Federal courts have also refused to equate structural similarity automatically with *prima facie* obviousness. *In re Langer*, 465 F.2d 896, 175 U.S.P.Q. 169 (C.C.P.A. 1972). In reversing a PTO conclusion of obviousness premised primarily on structural similarity, the CCPA in *In re Wagner*, 371 F.2d 877, 152 U.S.P.Q. 552 (C.C.P.A. 1967) found that the PTO had erred in failing to consider the biological or pharmaceutical properties of the claimed compounds. Although the prior art benzimidazole compounds had over eleven possible positions for substitution, nothing in the prior art suggested substituting the particular two positions claimed "*so as to enhance the biological or pharmaceutical activity of the compound* instead of diminishing it as in the [the prior art references]." *Id.* at 884, 152 U.S.P.Q. at 559. Thus, the court's decision makes clear that an obviousness determination based solely on

structural similarity violates the § 103 statutory mandate of considering the invention "as a whole".

The Office's reliance on *In re Lemin*, 141 U.S.P.Q. 814 (1964) to support *prima facie* obviousness (Final Action, page 11) also appears misplaced. In *In re Lemin*, the claimed compounds overlapped structurally and shared a common utility with the prior art compounds. *In re Lemin* is inapplicable to the present application where the cited references disclose structurally distinct compounds with dissimilar properties and utilities.

Moreover, this case is clearly distinguishable from *In re Dillon*, 919 F.2d 688, 16 U.S.P.Q. 1897 (Fed. Cir. 1990), in which the Federal Circuit, *en banc*, held that a hydrocarbon fuel composition containing tetra-orthoester was obvious in view of the prior art. In that case, the prior art expressly disclosed (1) hydrocarbon fuel compositions containing tri-orthoesters as dewatering agents, and (2) tri-orthoesters and tetra-orthoesters as both being water scavengers. Based on this combination of prior art, the court affirmed the Board's holding that it would have been obvious to substitute the tetra-orthoester for the tri-orthoester in the prior art hydrocarbon fuel composition. This suggested substitution was what Dillon was trying to claim. Notwithstanding the express teachings in *In re Dillon*, the court was divided with three judges dissenting.

In this case, unlike *In re Dillon*, there is no prior art teaching that the cited references' and applicant's compounds are equivalent as antifungal, herbicidal or neuroregenerative agents, or as treatments for asthma, anxiety or depression. Thus, there would have been no motivation to modify the cited referneces' compounds to arrive at applicant's claimed compounds.

Since the cited references fail to teach an equivalence between the asserted utilities of their disclosed compounds and that of applicant's claimed compounds, applicant's claimed compounds are not *prima facie* obvious in view of the cited references.

CONCLUSION

Based upon the foregoing amendments and remarks, the claimed subject matter is believed to be patentable. Accordingly, applicants respectfully request reconsideration and withdrawal of the outstanding rejections, and allowance of all pending claims.

The Examiner is welcome to telephone the undersigned attorney if she has any questions or comments.

Please charge any fees required by the filing of these papers to Lyon & Lyon LLP's Deposit Account No. **12-2475**.

Respectfully submitted,

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Dated: July 8, 2002

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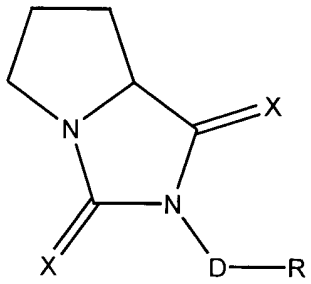
APPENDIX: MARKED-UP VERSION OF AMENDED CLAIM

1. (Amended) A compound of the formula:



[where] or a pharmaceutically acceptable salt, ester or solvate wherein:

each X independently is O, S, or NR_2;

R_2 is selected from the group consisting of cyano, nitro, hydrogen, C_1-C_4 alkyl, hydroxy, and C_1-C_4 alkoxy;

D is a direct bond or [a] C_1-C_8 alkyl or alkenyl;

R is selected from the group consisting of hydrogen, phenyl, biphenyl, cyclopropyl, cylobutyl, cyclopentyl, cycloheptyl, cyclooctyl, naphthyl, 1,2,3,4-tetrahydronaphthyl, indenyl, azulenyl, fluorenyl, anthracenyl, isoindolyl, indolinyl, benzofuranyl, benzothiophenyl, indazolyl, benzimidazolyl, tetrahydrofuranyl, tetrahydropyranyl, pyridyl, pyrrolyl, pyrrolidinyl, pyridinyl, pyrimidinyl, purinyl, quinolinyl, isoquinolinyl, tetrahydroquinolinyl, quinolizinyl, furyl, benzofuranyl, thiophenyl, imidazolyl, oxazolyl, benzoxazolyl, benzoxazinyl, thiazolyl, isoxazolyl, isotriazolyl, oxadiazolyl, triazolyl, thiadiazolyl, pyridazinyl, pyrimidinyl, pyrazinyl, triazinyl, trithianyl, indolizinyl, pyrazolyl, pyrazolinyl, pyrazolidinyl, benzopyranyl, thienyl, tetrahydroisoquinolinyl, cinnolinyl, phthalazinyl, quinazolinyl, quinoxalinyl,

naphthyridinyl, pteridinyl, carbazolyl, phenazinyl, phenothiazinyl, phenoxazinyl, and adamantyl;

wherein R may be optionally substituted with one substituent which is selected from the group consisting of [hydrogen,] halo, hydroxyl, nitro, trifluoromethyl, C_1-C_6 straight or branched chain alkyl, C_2-C_6 straight or branched chain alkenyl, C_1-C_4 alkoxy, C_2-C_4 alkenyloxy, phenyl, phenoxy, benzyloxy, and amino;

[or a pharmaceutically acceptable salt, ester, or solvate thereof;]

(1) wherein when R is hydrogen, then D is [a] C_5-C_7 alkyl or C_5-C_8 alkenyl;

(2) wherein when R is phenyl and D is a bond, then R [must be] is substituted with phenyl, hydroxyl, trifluoromethyl, C_2-C_6 straight or branched chain alkyl or alkenyl, C_3-C_4 alkoxy, [or] C_2-C_4 alkenyloxy, phenoxy, or benzyloxy;

(3) wherein when R is 4-trifluoromethylphenyl, then both X substituents [must be] are O;

(4) wherein when both X substituents are O and D is C_2 alkyl, then R is not phenyl substituted with 4-nitro or 4-amino;

(5) wherein when both X substituents are O and R is H, D is not C_1-C_8 alkyl;

(6) wherein when both X substituents are O and D is C_1 alkyl, R is not phenyl;

(7) wherein when both X substituents are O and D is a direct bond, then R is not phenyl substituted with 3-trifluoromethyl, 4-methoxy, 4-fluoro, 4-chloro, 3,5-dichloro, 4-methyl, 4-ethoxy, 4-bromo or 3,4-dichloro;

(8) wherein when one X is O, the other X is S, and D is a direct bond, then R is not phenyl substituted with 3-trifluoromethyl, 4-methoxy, 4-bromo, 3,4-dichloro, 4-methyl, 4-chloro, 4-nitro or 3,5-dichloro; and

(9) wherein when both X substituents are O and D is C_3 straight chain alkyl, then D is not phenyl substituted with 3-methoxy.